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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,923	12/19/2001	James Thacker	8109.003.USDV	9929

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/020,923	THACKER, JAMES	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11, 29, 30, and 33-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,29,30 and 33-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Amendment Entry

2. Claims 1-10, 12-28 and 31-32 have been cancelled. Claims 11, 29-30 and 33-47 are under consideration in this office action.

Response to Arguments

3. Applicant's arguments filed September 17, 2007 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 11, 29-30 and 33-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shih et al.,(US Patent 4,026,767 published May 31, 1977) in view of Litman et al., (US Patent 4,374,925 published February 22, 1983).

Claim 11 is drawn to a method for detecting 10,000 cfu/ml or less of microorganisms comprising: incubating the microorganisms for an incubation period of less than eight hours with a nutrient medium containing a predetermined amount of a viability substrate, wherein metabolism of said viability substrate by the microorganisms produces a viability marker; digesting the microorganism; incubating the digested microorganisms with a primary antibody specific for the viability marker; conjugating the primary antibody to a reporter molecule to form a reporter-primary antibody complex; detecting reporter molecules that form reporter-primary antibody complex and determining the amount microorganisms from the reporter-primary antibody complexes detected, wherein the microorganisms are bacteria.

Claim 37 is drawn to a method for detecting 1,000 cfu/ml or less of microorganisms comprising: incubating the microorganisms for an incubation period of less than two hours with a nutrient medium containing a predetermined amount of a viability substrate, wherein metabolism of said viability substrate by the microorganisms produces a viability marker; digesting the microorganism; incubating the digested microorganisms with a primary antibody specific for the viability marker; conjugating the primary antibody to a reporter molecule to form a reporter-primary antibody complex; detecting reporter molecules that form reporter-primary antibody complex and

determining the amount microorganisms from the reporter-primary antibody complexes detected, wherein the microorganisms are bacteria.

Claim 42 is drawn to a method for detecting 10,000 cfu/ml or less of microorganisms comprising: incubating the microorganisms for an incubation period of less than thirty minutes with a nutrient medium containing a predetermined amount of a viability substrate, wherein metabolism of said viability substrate by the microorganisms produces a viability marker; digesting the microorganism; incubating the digested microorganisms with a primary antibody specific for the viability marker; conjugating the primary antibody to a reporter molecule to form a reporter-primary antibody complex; detecting reporter molecules that form reporter-primary antibody complex and determining the amount microorganisms from the reporter-primary antibody complexes detected, wherein the microorganisms are bacteria. The dependant claims are drawn to incubation periods, reporter molecules, sample types and the population of microorganisms.

Shih et al., teach detecting bacteria comprising: incubating the microorganisms for a few hours with a nutrient medium containing a predetermined amount of a viability substrate (col.4-5, lines 68-2), wherein metabolism of said viability substrate by the microorganisms produces a blue color or a viability marker (col.5, lines 3-5). Shih et al., teach the presence of bacteria in blood or other fluids comprising introducing the material to be tested into a nutrient medium containing a ditetrazolium chloride which converts to detectable blue color component in response to dehydrogenase reduction which takes place when microorganisms are present (col.1, lines 60-68). The effective

substrate is the enzymatic lactic dehydrogenase (col.4, lines 3-5). Shih et al., teach a simple and effective test which can be carried out quickly and efficiently and it is understood that changes may be made in the details of the operations without departing from the spirit of the invention (col. 5, lines 25-32). However Shih et al., do not teach digesting the microorganism; incubating the digested microorganisms with a primary antibody specific for the viability marker; conjugating the primary antibody to a reporter molecule to form a reporter-primary antibody complex; detecting reporter molecules that form reporter-primary antibody complex and determining the amount microorganisms from the reporter-primary antibody complexes detected, conjugation of primary antibodies with reporter molecules and their detection.

Litman et al, teach preparation of analyte microorganisms by means of digestion via lysis, grounding, fragmentation or extraction (col. 14, lines 65-68). Litman et al., teach binding pair where one member is an antibody receptor, wherein a receptor is any compound or composition capable of recognizing the ligand molecule (col. 20-24); and the other member of the pair is bound to a reporter (label) capable of providing a detectable signal (col. 1, lines 15-19). Litman et al., teach the antibody specifically binds the enzyme (viability marker) and is then conjugated to a reporter (see Table 1). Table IV teach enzymes and exemplary reaction including lactate dehydrogenase reactions (col. 25-26). Litman et al., teach reporter labels such as radiolabels, enzymes, particles and fluorescent molecules (col. 2, lines 34-36). Table 1 illustrates different binding pair complexes and means by which a signal producing systems and reagents are combinable, thereby teaching reporter-antibody complexes. Litman et al., teach that a

main consideration for using immunoassays is their sensitivity (col. 2, lines 36-38). Litman et al., teach that immunoassays measure extremely small amounts of ligand with high levels of accuracy and minimize or remove interference from other materials (col.2, lines 26-35). Furthermore, immunoassays provide simple protocols, ease of measurement, reproducible results, and sensitivity to extraneous factors (col.2, lines 35-44).

Therefore it would have been prima facie obvious at the time of applicants' invention to apply Litman et al's digestion, incubation, conjugation and detection to an effective method for detecting 10,000 cfu/ml or less of bacteria as taught by Shih et al., in order to provide a simple, effective, quick and efficient method of bacterial detection. One of ordinary skill in the art would have a reasonable expectation of success by incorporating a digestion step; incubation step; conjugation step; and detection steps as taught by Litman et al., into the method of Shih et al., because Litman et al., already teach no more than routine skill is required to sensitively detect lactic dehydrogenase reaction products (i.e., the viability marker) of Shih et al., using reporter-antibody complexes. Moreover, no more than routine skill would have been required to incorporate Litman et al's additional method of detection steps which are known to detect extremely small amounts of ligand with high levels of accuracy and minimize or remove interference from other materials into the method of Shih et al., since Shih et al., teach the desirability to determine the presence/amount of bacteria in a sample using a viability substrate without the prolonged time periods associated with culturing blood. Furthermore, Litman et al., disclose that immunoassays advantageously achieve

benefits by providing simple protocols, easy measurements and reproducible results. Finally, the limitations drawn to the specific detection limitations are viewed as merely optimizing the experimental parameters and not imparting patentability; thus no more than routine skill would have been required to acquire the recited detection limitations in the well known method of detection as taught by Shih et al., in view of Litman et al.

Response to Arguments

5. Applicant's arguments filed September 17, 2007 have been fully considered but they are not persuasive.

The rejection of claims 11, 29-30 and 33-47 under 35 U.S.C. 103(a) as being unpatentable over Shih et al.,(US Patent 4,026,767 dated May 31, 1977) in view of Litman et al., (US Patent 4,374,925 dated February 22, 1983) is maintained. Applicants argue that the Shih and Litman references were filed over 20 years ago and because of the age of the reference the instantly claimed process must be surprising and unexpected. In response to applicant's argument based upon the age of the references, contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). However, the mere age of the references do not prevent them from teaching the instantly claimed invention. The references teach incubating the microorganisms for an incubation period of less than eight hours with a nutrient medium

containing a predetermined amount of a viability substrate, the production of a viability marker; digesting the bacteria; incubation of the digested bacteria with a primary antibody specific for the viability marker; conjugating the primary antibody to a reporter molecule to form a reporter-primary antibody complex; detecting reporter molecules that form reporter-primary antibody complex and determining the amount bacterium from the reporter-primary antibody complexes detected. Therefore applicants' arguments are not persuasive.

Applicants' assert that Because Shih et al., do not discloses the digestion step or the use of antibodies, the references fail to teach the invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). However, in this case, it would have been prima facie obvious at the time of applicants' invention to apply Litman et al's digestion, incubation, conjugation and detection to an effective method for detecting 10,000 cfu/ml or less of bacteria as taught by Shih et al., in order to provide a simple, effective, quick and efficient method of bacterial detection. One of ordinary skill would have a reasonable expectation of success by incorporating a digestion step; incubation step; conjugation step; and detection steps as taught by Litman et al., into the method of Shih et al., because Litman et al., already teach no more than routine skill is required to sensitively detect lactic dehydrogenase reaction

products (i.e., the viability marker) of Shih et al., using reporter-antibody complexes. Therefore applicants' argument is not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would be obvious to a person of ordinary skill in the art at the time the invention was made to modify the method taught by Shih et al., by adding additional steps to amplify the signal generated because it would help to generate more sensitive immunoassays as taught by Litman et al. Furthermore, Shih et al., teach lactic dehydrogenase reactions to produce the viability markers; Litman et al., teach the specific detection of lactic dehydrogenase reaction products, therefore Litman et al., teach immuno-detection of the exact same product. Therefore, one of ordinary skill in the art would have a reasonable expectation of success because one of ordinary skill in the art would have been motivated to make such changes in method since it is well known in the art of immunoassays to use antibodies specific and sensitive within the colorimetric assays taught by Shih et al.

Applicants' urge that the claimed invention provides exponential amplification of sensitivity and speed of detection for microorganisms. Applicants' assert that neither

Shih nor Litman, alone or ill combination, achieve the same levels of sensitivity (detection of 10.000 cfu/mL or less 0f microorganisms) as does the claimed invention, and neither Shih nor Litman, alone or in combination, disclose or suggest the methods for achieving sensitivity of the claimed invention. However, in response to applicant's argument, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and In re Otto, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). In this case, the method for detection as taught by Shih et al., and Litman et al., is capable of detecting less than 10,000 cfu of microorganisms/ml and taking less than two hours to perform. No steps within the instantly claimed method will prevent the prior art method from detecting 10,000 cfu or less of the microorganisms. Moreover, applicants' have not presented any evidence to the contrary. Merely stating that the prior art method is not capable of detecting less than 10,000 cfu of microorganisms/ml absent scientific evidence is not persuasive.

Furthermore, Shih et al., in view of Litman et al., teach detection of extremely small amounts. It is noted that limitations such as different detection limitations are viewed as limitations not imparting patentability. There is no evidence that these limitations provide unexpected results, as increased sensitivity is not unexpected. All the components act in a traditional and expected manner, furthermore all the process steps provide expected functionalities. A process which is directed to a selection of variable

within the broad teachings of the prior art is not patentable if the results achieved vary merely in degree from that obtained in the prior art. Expected beneficial results are evidence of obviousness. Therefore, applicants' arguments are not persuasive.

Applicants' urge that neither Shih nor Litman disclose or suggest employing digestion reagents comprising, for example, lysosome, to digest the microorganisms which have been marked with a viability substrate to produce marked cell debris, which is then detected (see specification pages 9-10). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., digestion reagents comprising, lysosome are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore applicants' arguments regarding the lysosome activity are not persuasive.

Therefore the rejections of record are maintained.

Conclusion

6. No claims allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Shanon Foley, can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
February 5, 2008

/Mark Navarro/

Primary Examiner, Art Unit 1645